

08/11/200417:12Print selected from Online session

Seminar Schedule - N. America

NEWS 2 "Ask CAS" for self-help around the clock
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resulting in a closer connection to BABS
NEWS 4 AUG 02 IFIPAT/IFIUDB/IFICDB reloaded with new search and display
fields
NEWS 5 AUG 02 CAPLUS and CA patent records enhanced with European and Japan
Patent Office Classifications
NEWS 6 AUG 02 The Analysis Edition of STN Express with Discover!
(Version 7.01 for Windows) now available
NEWS 7 AUG 27 BIOCOMMERCE: Changes and enhancements to content coverage
NEWS 8 AUG 27 BIOTECHABS/BIOTECHDS: Two new display fields added for legal
status data from INPADOC
NEWS 9 SEP 01 INPADOC: New family current-awareness alert (SDI) available
NEWS 10 SEP 01 New pricing for the Save Answers for SciFinder Wizard within
STN Express with Discover!
NEWS 11 SEP 01 New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS 12 SEP 27 STANDARDS will no longer be available on STN
NEWS 13 SEP 27 SWETSCAN will no longer be available on STN
NEWS 14 OCT 28 KOREAPAT now available on STN

NEWS EXPRESS OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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=> index bioscience

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AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS,
BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB,
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=> bcl-2 and nmr and apoptosis

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22 FILE BIOSIS

12 FILES SEARCHED...

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2 FILE BIOTECHDS
8 FILE BIOTECHNO
10 FILE CANCERLIT
29 FILE CAPLUS
1 FILE CEABA-VTB
1 FILE CIN
3 FILE DDFU
3 FILE DISSABS
5 FILE DRUGU

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3 FILE FEDRIP
1 FILE FSTA
6 FILE IFIPAT
4 FILE JICST-EPLUS
6 FILE LIFESCI
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L1 QUE BCL-2 AND NMR AND APOPTOSIS

=> file caplus biosis medline

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FILE 'MEDLINE' ENTERED AT 17:00:35 ON 08 NOV 2004

=> dup remove

ENTER L# LIST OR (END):end

=> bcl-2 and nmr and apoptosis

L2 76 BCL-2 AND NMR AND APOPTOSIS

=> dup remove

ENTER L# LIST OR (END):12

PROCESSING COMPLETED FOR L2

L3 43 DUP REMOVE L2 (33 DUPLICATES REMOVED)

=> d ti 23-43

L3 ANSWER 23 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

TI Novel chemically-stabilized helices of the **BCL-2** family induce **apoptosis** of leukemia cells.

L3 ANSWER 24 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

TI Phospholipid scramblase transport system-based method for targeting chemical compounds to cells, pharmaceutical compositions, and therapeutic and diagnostic use

L3 ANSWER 25 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of amino acid derivatives used as perturbed membrane-binding compounds for diagnostic and therapeutic applications

L3 ANSWER 26 OF 43 MEDLINE on STN

TI The apoptotic protein tBid promotes leakage by altering membrane curvature.

L3 ANSWER 27 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 11

TI Novel Polyphenol Molecule Isolated from Licorice Root (*Glycyrrhiza glabra*) Induces **Apoptosis**, G2/M Cell Cycle Arrest, and **Bcl-2** Phosphorylation in Tumor Cell Lines

L3 ANSWER 28 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

TI A view to a kill: Ligands for **Bcl-2** family proteins.

L3 ANSWER 29 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 12

TI Changes in phosphate metabolism in thymoma cells suggest mechanisms for resistance to dexamethasone-induced **apoptosis**. A 31P NMR spectroscopic study of cell extracts

L3 ANSWER 30 OF 43 MEDLINE on STN

TI Backbone dynamics of the 8 kDa dynein light chain dimer reveals molecular basis of the protein's functional diversity.

L3 ANSWER 31 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 13

TI Novel substituted methylenedioxy lignan suppresses proliferation of cancer cells by inhibiting telomerase and activation of c-myc and caspases leading to **apoptosis**

L3 ANSWER 32 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 14

TI What's in the 'BAG'? - a functional domain analysis of the BAG-family proteins

L3 ANSWER 33 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 15

TI Discovery of Small-Molecule Inhibitors of **Bcl-2** through Structure-Based Computer Screening

- L3 ANSWER 34 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Bax and other pro-apoptotic Bcl-2 family "killer-proteins" and their victim, the mitochondrion.
- L3 ANSWER 35 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 16
TI Identification of small-molecule inhibitors of interaction between the BH3 domain and Bcl-XL
- L3 ANSWER 36 OF 43 MEDLINE on STN
TI NMR studies of the anti-apoptotic protein Bcl-xL in micelles.
- L3 ANSWER 37 OF 43 MEDLINE on STN
TI Rationale for Bcl-xL/Bad peptide complex formation from structure, mutagenesis, and biophysical studies.
- L3 ANSWER 38 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Targeting the mitochondrial redox state of leukemia and lymphoma cells with PK11195 for effective therapy.
- L3 ANSWER 39 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Assessing pore formation by BCL-2 during apoptosis in cell lines and human leukemic cells: Cysteine 158 in the alpha 5 helical loop is in an aqueous environment.
- L3 ANSWER 40 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 17
TI Refolding, Purification, and Characterization of a Loop Deletion Mutant of Human Bcl-2 from Bacterial Inclusion Bodies
- L3 ANSWER 41 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 18
TI Recombinant mouse Bcl-2(1-203). Two domains connected by a long protease-sensitive linker
- L3 ANSWER 42 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 19
TI Detection of apoptotic cell death by proton nuclear magnetic resonance spectroscopy
- L3 ANSWER 43 OF 43 MEDLINE on STN
TI X-ray and NMR structure of human Bcl-xL, an inhibitor of programmed cell death.

=> ti 1-23

L4 1 TI 1-23

=> d ti 1-23

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

TI Separating commercially pure vanadium from crude ferrophosphorus

=> bcl-2 and nmr and apoptosis

L5 76 BCL-2 AND NMR AND APOPTOSIS

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L6 43 DUP REMOVE L5 (33 DUPLICATES REMOVED)

=> d ti 1-23

L6 ANSWER 1 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Conversion of apoptotic proteins

L6 ANSWER 2 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Methods of identifying agents that alter association of Bcl-2 and AES, alter
Bcl-2 transcription, and/or modulate cell death, and
therapeutic uses

L6 ANSWER 3 OF 43 MEDLINE on STN
TI Conformation of membrane-associated proapoptotic tBid.

L6 ANSWER 4 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Changes in phosphate metabolism in thymoma cells suggest mechanisms for
resistance to dexamethasone-induced **apoptosis**. A 31P NMR
spectroscopic study of cell extracts. [Erratum to document cited in
CA138:036909]

L6 ANSWER 5 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Solution Conformations of Wild-Type and Mutated Bak BH3 Peptides via
Dynamical Conformational Sampling and Implication to Their Binding to
Antiapoptotic **Bcl-2** Proteins

L6 ANSWER 6 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
TI Targeting **Apoptosis** via Chemical Design Inhibition of
Bid-Induced Cell Death by Small Organic Molecules

L6 ANSWER 7 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
TI Divergence of Genbank and human tumor **Bcl-2** sequences
and implications for binding affinity to key apoptotic proteins

L6 ANSWER 8 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
TI Localization of dynein light chains 1 and 2 and their pro-apoptotic
ligands

L6 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
TI Rational design and real time, in-cell detection of the proapoptotic
activity of a novel compound targeting Bcl-XL

L6 ANSWER 10 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
TI Small-molecule inhibitors of **Bcl-2** protein

L6 ANSWER 11 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
TI Structural studies of **apoptosis** and ion transport regulatory
proteins in membranes

L6 ANSWER 12 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
TI Defining the p53 DNA-binding domain/Bcl-xL-binding interface using

NMR

- L6 ANSWER 13 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
TI Overexpression of catalase or **Bcl-2** alters glucose and energy metabolism concomitant with dexamethasone resistance
- L6 ANSWER 14 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Humanin protein interactions with Bax and Bid and their use for identifying modulators of **apoptosis**
- L6 ANSWER 15 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Solution Structure of Human BCL-w: Modulation of Ligand Binding by the C-Terminal Helix
- L6 ANSWER 16 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Discovery, Characterization, and Structure-Activity Relationships Studies of Proapoptotic Polyphenols Targeting B-Cell Lymphocyte/Leukemia-2 Proteins
- L6 ANSWER 17 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Cyclic AMP reverses radiocontrast media-induced **apoptosis** in LLC-PK1 cells by activating A kinase/PI3 kinase
- L6 ANSWER 18 OF 43 MEDLINE on STN
TI Unique structural features of a **BCL-2** family protein CED-9 and biophysical characterization of CED-9/EGL-1 interactions.
- L6 ANSWER 19 OF 43 MEDLINE on STN
TI Solution structure of the BHRF1 protein from Epstein-Barr virus, a homolog of human **Bcl-2**.
- L6 ANSWER 20 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Interaction of BID, a pro-apoptotic **BCL-2** family member, with lipid membranes: A site-directed spin labeling Study.
- L6 ANSWER 21 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9
TI Overexpression of catalase or **Bcl-2** delays or prevents alterations in phospholipid metabolism during glucocorticoid-induced **apoptosis** in WEHI7.2 cells
- L6 ANSWER 22 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
TI Structure determination, **apoptosis** induction, and telomerase inhibition of CFP-2, a novel lichenin from *Cladonia furcata*
- L6 ANSWER 23 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Novel chemically-stabilized helices of the **BCL-2** family induce **apoptosis** of leukemia cells.

=> d ab bib 20, 22, 23, 28, 39, 40

- L6 ANSWER 20 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:422995 BIOSIS
DN PREV200300422995
TI Interaction of BID, a pro-apoptotic **BCL-2** family member, with lipid membranes: A site-directed spin labeling Study.

AU Oh, Kyoung Joon [Reprint Author]; Meyer, Natalie [Reprint Author];
Korsmeyer, Stanley J. [Reprint Author]
CS Harvard Medical School, Dana-Farber Cancer Institute, HHMI, 44 Binney St.,
Smith 758, Boston, MA, 02115-7008, USA
SO Biophysical Journal, (February 2003) Vol. 84, No. 2 Part 2, pp. 205a-206a.
print.
Meeting Info.: 47th Annual Meeting of the Biophysical Society. San
Antonio, TX, USA. March 01-05, 2003. Biophysical Society.
ISSN: 0006-3495 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Sep 2003
Last Updated on STN: 17 Sep 2003

L6 ANSWER 22 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
AB A great deal of exptl. evidence has accumulated in the past several
decades, suggesting that polysaccharides have wide bioactivities.
Cladonia furcata polysaccharide, CFP-2, a water-soluble lichenin with a mean
Mr 7.6 + 104, was first obtained by 0.25 M NaOH solution extraction, ethanol
precipitation, DEAE-cellulose, and Sephadex G-200 column chromatog. Gas
chromatog. of acid hydrolyzate of CFP-2 suggested that it was composed of
D-glucose, D-galactose, and D-mannose in the molar ratios of 8:1:1.
Periodate oxidation, Smith degradation, IR, and NMR spectroscopy anal.
revealed that CFP-2 had a backbone consisting of α -(1 \rightarrow 3) and
 α -(1 \rightarrow 4)-linked D-glucopyranosyl residues substituted at O-6
with β -(1 \rightarrow 6)-linked D-galactopyranosyl residue and
 α -(1 \rightarrow 6)-linked D-mannopyranosyl residue. CFP-2 was able to
reduce viability of cultured HL-60 and K562 cells. The antiproliferative
properties of CFP-2 appeared to be attributable to its induction of
apoptotic cell death as determined by ultrastructural change, internucleosomal
DNA fragmentation, and increased proportion of the subdiploid cell
population. To elucidate mol. events in the **apoptosis**, protein
expressions of Bcl-2, Bax, Fas, and FasL were measured
by Western blotting using specific antibodies in HL-60 cells. The level
of Bcl-2 remained largely unchanged, but the Bax, Fas,
and FasL expression showed up-regulation. Moreover, the telomerase
activity analyzed by TRAP-ELISA assay in HL-60 cells treated with CFP-2
decreased as compared with the untreated control cells. These results
suggest that CFP-2 could have a possible cancer therapeutic potential.

AN 2003:567406 CAPLUS
DN 139:334572
TI Structure determination, **apoptosis** induction, and telomerase
inhibition of CFP-2, a novel lichenin from Cladonia furcata
AU Lin, Xin; Cai, Yu-Jun; Li, Zhi-Xiao; Chen, Qian; Liu, Zhong-Li; Wang, Rui
CS School of Life Science, Department of Biochemistry and Molecular Biology,
Lanzhou University, Lanzhou, 730000, Peop. Rep. China
SO Biochimica et Biophysica Acta (2003), 1622(2), 99-108
CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 23 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN
AB Faulty regulation of apoptotic pathways is a seminal event in the
pathogenesis of a wide variety of hematologic, oncologic, and other

diseases. **Apoptosis** is governed by the **BCL-2** family of pro- and anti-apoptotic proteins, which form a complex network of checks and balances that dictate cell fate. **BCL-2**, for example, is a survival protein whose overproduction can facilitate pathologic cell survival. Anti-apoptotic proteins, such as **BCL-2** and **BCL-XL**, and pro-apoptotic proteins, such as **BAK** and **BAX**, share sequence conservation in multiple "**BCL-2** homology" (BH) domains. These "multidomain" apoptotics exert their roles as guardian or executioner at mitochondrial and endoplasmic reticulum membranes, receiving regulatory signals from another class of pro-apoptotic proteins, characterized by homology in the BH3-domain only. Deletion and mutagenesis studies determined that the amphipathic alpha-helical BH3 segment of pro-apoptotic family members functions as a critical death domain. Whereas peptides modeled after BH3 domains retain select in vitro biochemical activities, their in vivo utility is compromised by loss of helical secondary structure, susceptibility to proteolytic degradation, and inability to penetrate intact cells. We developed and applied a chemical strategy for generating highly specific and stable peptidic compounds that preserve both the primary and secondary structure of biologically active apoptotic peptides, in order to maximize their potential as therapeutic reagents and as in vivo biological tools to elucidate apoptotic pathways. We employed a synthetic crosslinking strategy to generate a panel of "Stabilized Alpha-Helices of BH3-domains" or SAHBs modeled after the BH3 domain of BID, a pro-apoptotic family member capable of activating mitochondrial cell death through interactions with both pro- and anti-apoptotic multidomain proteins. Circular dichroism studies revealed dramatic enhancement of SAHB secondary structure in solution, with several compounds displaying a more than 5-fold increase in percent helicity compared to the unmodified BID BH3 peptide. SAHBs are likewise more resistant to proteolytic degradation as determined by trypsin digestion kinetic analyses. In in vitro binding assays, SAHBs display increased **BCL-2** binding affinity. Two-dimensional 1H-15N Heteronuclear Single Quantum Correlation Nuclear Magnetic Resonance (HSQC NMR) spectra confirmed that SAHBs specifically engage the physiologic BH3-binding site of multidomain anti-apoptotic proteins. SAHBs induce rapid release of cytochrome c from purified mouse liver mitochondria, but have no effect on mitochondria lacking BAK/BAX, confirming the specificity of SAHB activity in triggering mitochondrial **apoptosis**. The cell permeability of SAHBs was demonstrated by tracking fluorescein-labeled SAHBs in cultured cells by FACS analysis and confocal microscopy. Furthermore, SAHBs activate **apoptosis** in cultured B-, T-, and mixed-lineage leukemia cells. The specificity of SAHB activity in inducing leukemia cell **apoptosis** was confirmed by the inability of mutant SAHBs, incorporating a single point mutation known to abolish BH3-domain activity, to have any effect on the cultured cells. These data indicate that SAHBs have the potential to serve as biological tools to dissect and manipulate apoptotic pathways in vivo in normal and malignant cells.

AN 2004:180831 BIOSIS

DN PREV200400180880

TI Novel chemically-stabilized helices of the **BCL-2** family induce **apoptosis** of leukemia cells.

AU Walensky, Loren D. [Reprint Author]; Escher, Iris; Malia, Thomas J.; Wagner, Gerhard; Verdine, Gregory L.; Korsmeyer, Stanley J.

CS Department of Pediatric Hematology/Oncology, Dana Farber Cancer Institute/Children's Hospital Boston, Harvard Medical School, Boston, MA, USA

SO Blood, (November 16 2003) Vol. 102, No. 11, pp. 5a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology.

San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004

L6 ANSWER 28 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
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AN 2002:500148 BIOSIS

DN PREV200200500148

TI A view to a kill: Ligands for **Bcl-2** family proteins.

AU Rutledge, Stacey E. [Reprint author]; Chin, Jason W.; Schepartz, Alanna
[Reprint author]

CS Department of Chemistry, Yale University, PO Box 208107, New Haven, CT,
06520-8107, USA

SO Current Opinion in Chemical Biology, (August, 2002) Vol. 6, No. 4, pp.
479-485. print.
ISSN: 1367-5931.

DT Article
General Review; (Literature Review)

LA English

ED Entered STN: 25 Sep 2002

Last Updated on STN: 25 Sep 2002

L6 ANSWER 39 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
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AB The ability of the **Bcl-2** family of anti-apoptotic proteins to prevent programmed cell death has been attributed to multiple mechanisms, including binding pro-apoptotic proteins as well as the formation of pores. The evidence for the latter mechanism is extensive but indirect and includes the presence of alpha helical domains (designated alpha-5 and alpha-6) that are similar to several bacterial pore forming domains, as determined by NMR and X-ray crystallography of recombinant Bcl-XL without the hydrophobic insertion tail; the ability of recombinant Bcl-XL and **Bcl-2** to form ion conducting channels in artificial lipid bi-layers; and the loss of anti-apoptotic activity of a Bcl-XL mutant in which a portion of the putative pore forming domain is altered. To assess the conformation of **Bcl-2**, we have examined the local environment of cysteine 158 located in the alpha-5 helix near the base of the pore forming region, and cysteine 229 located in the hydrophobic insertion sequence, using the lipid impermeant cysteine modifying agent iodoacetyl amino stilbene disulfonic acid (IASD). When human **Bcl-2** is translated in vitro in the absence of membranes, both cysteines are modified by IASD, albeit with different kinetics. In the presence of membranes, cysteine 229 is not labelled by IASD, consistent with our previous work demonstrating that the insertion sequence is necessary and sufficient for insertion into multiple intracellular membranes. In this circumstance, cysteine 158 is still modifiable by IASD. In the Rat 1/myc model system of **apoptosis**, cysteine 158 is accessible to IASD in untreated cells, and early during serum starvation-induced **apoptosis** at time points during which **Bcl-2** is protective. By contrast, late in **apoptosis** when **Bcl-2** has lost its effect, this cysteine is no longer modifiable. Cysteine 229 remains inaccessible under all three conditions, consistent with the expected membrane topology of **Bcl-2** in cells. Ongoing experiments will assess whether

a functionally active Bcl-XL mutant targeted to the endoplasmic reticulum in human breast cancer MCF7 cells, and endogenous Bcl-2 in the lymphocytes of patients with B cell chronic lymphocytic leukemia adopt a similar configuration. Our results suggests that the alpha-5 helical loop is not in a lipid environment while Bcl-2 is functioning to prevent apoptosis.

AN 2001:289142 BIOSIS

DN PREV200100289142

TI Assessing pore formation by BCL-2 during apoptosis in cell lines and human leukemic cells: Cysteine 158 in the alpha 5 helical loop is in an aqueous environment.

AU Leber, B. [Reprint author]; Kim, P. [Reprint author]; Falcone, D. [Reprint author]; Annis, M. [Reprint author]; Andrews, D. W. [Reprint author]

CS Medicine, McMaster University, Hamilton, ON, Canada

SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 174b. print. Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 20 Jun 2001

Last Updated on STN: 19 Feb 2002

L6 ANSWER 40 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 17

AB This report describes the cloning of recombinant human Bcl-2, in which the putative disordered loop region has been replaced with a flexible linker and the hydrophobic C-terminus has been replaced with a 6xHis tag (Bcl-2(6-32)-AAAA-Bcl-2(86-206)-HHHHHH, abbreviation rhBcl-2; amino acid numbering excludes the initiating methionine). This protein was expressed in Escherichia coli, where it accumulated in insol. form in inclusion bodies. After lysis, the washed inclusion bodies were solubilized and an L-arginine assisted protein refolding route was employed to obtain biol. active protein. RhBcl-2 was purified further by nickel chelate chromatog. to give protein of >95% purity, with an overall yield of 5 mg per g of E. coli cell paste. Edman sequencing showed that .apprx.90% of the rhBcl-2 retained the initiating methionine residue. Anal. size exclusion chromatog. suggested that the refolded and purified rhBcl-2 was monomeric in nondenaturing solution. Purified protein had an affinity for a Bax BH3 domain peptide comparable to that for in vivo folded recombinant human Bcl-2 and suppressed caspase activation in a cell-free assay for apoptosis. 1H NMR spectroscopy of rhBcl-2, both free and complexed with the Bax BH3 domain peptide, provided further evidence for the structural and functional integrity of the refolded protein. These findings parallel and extend those of Muchmore et al., who found that a loop deletion mutant of human Bcl-XL retained anti-apoptotic function. (c) 1999 Academic Press.

AN 1999:134162 CAPLUS

DN 131:4284

TI Refolding, Purification, and Characterization of a Loop Deletion Mutant of Human Bcl-2 from Bacterial Inclusion Bodies

AU Anderson, Malcolm; Blowers, David; Hewitt, Neil; Hedge, Philip; Breeze, Alexander; Hampton, Ian; Taylor, Ian

CS Target Discovery, Zeneca Pharmaceuticals, Macclesfield, SK10 4TG, UK

SO Protein Expression and Purification (1999), 15(2), 162-170

CODEN: PEXPEJ; ISSN: 1046-5928

PB Academic Press

08/11/200417:12Print selected from Online session

DT Journal

LA English

RE:CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
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=> NMR and Bcl-2

```
1 FILE ADISINSIGHT
2 FILE AGRICOLA
1 FILE BIOENG
39 FILE BIOSIS
4 FILE BIOTECHABS
4 FILE BIOTECHDS
10 FILE BIOTECHNO
17 FILE CANCERLIT
49 FILE CAPLUS
1 FILE CEABA-VTB
2 FILE CIN
23 FILES SEARCHED...
3 FILE DDFU
5 FILE DISSABS
5 FILE DRUGU
25 FILE EMBASE
22 FILE ESBIODASE
3 FILE FEDRIP
36 FILES SEARCHED...
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10 FILE IFIPAT
7 FILE JICST-EPLUS
8 FILE LIFESCI
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L1 QUE NMR AND BCL-2

=> NMR p Bcl-2

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32 FILES SEARCHED...
68 FILES SEARCHED...
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L2 QUE NMR P BCL-2

=> NMR and Bcl-2 and TR3

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1 FILE CAPLUS
27 FILES SEARCHED...
1 FILE IFIPAT
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4 FILE USPATFULL
69 FILES SEARCHED...
1 FILE WPIDS
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1 FILE WPINDEX

7 FILES HAVE ONE OR MORE ANSWERS, 75 FILES SEARCHED IN STNINDEX

L3 QUE NMR AND BCL-2 AND TR3

=> file biotechabs uspatfull caplus

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FULL ESTIMATED COST

6.27

6.48

FILE 'BIOTECHABS' ACCESS NOT AUTHORIZED

FILE 'USPATFULL' ENTERED AT 13:31:24 ON 08 NOV 2004

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=> NMR and Bcl-2 and TR3

L4 5 NMR AND BCL-2 AND TR3

=> dup remove

ENTER L# LIST OR (END):L4

PROCESSING COMPLETED FOR L4

L5 5 DUP REMOVE L4 (0 DUPLICATES REMOVED)

=> d ti 1-5

L5 ANSWER 1 OF 5 USPATFULL on STN

TI Conversion of apoptotic proteins

L5 ANSWER 2 OF 5 USPATFULL on STN

TI Therapeutic treatment methods

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

TI Conversion of apoptotic proteins

L5 ANSWER 4 OF 5 USPATFULL on STN

TI Blood cell deficiency treatment method

L5 ANSWER 5 OF 5 USPATFULL on STN

TI Isolated nucleic acid encoding a ubiquitous nuclear receptor

=> d ab bib 2, 4, 5

L5 ANSWER 2 OF 5 USPATFULL on STN

AB The invention relates to the use of compounds to ameliorate or treat an condition such as a cystic fibrosis, neutropenia or other exemplified conditions. Exemplary compounds that can be used include 3 β -hydroxy-17 β -aminoandrost-5-ene, 3 β -hydroxy-16 α -fluoro-17 β -aminoandrost-5-ene, 3 α -hydroxy-16 α -fluoro-17 β -aminoandrost-5-ene, 3 β -hydroxy-16 β -fluoro-17 β -aminoandrost-5-ene, 1 α ,3 β -dihydroxy-4 α -fluoroandrost-5-ene-17-one, 1 α ,3 β ,17 β -trihydroxy-4 α -fluoroandrost-5-ene, 1 β ,3 β -dihydroxy-6 α -bromoandrost-5-ene,

1 α -fluoro-3 β ,12 α -dihydroxyandrost-5-ene-17-one,
1 α -fluoro-3 β ,4 α -dihydroxyandrost-5-ene and
4 α -fluoro-3 β ,6 α ,17 β -trihydroxyandrostane.
AN 2004:179017 USPATFULL
TI Therapeutic treatment methods
IN Reading, Christopher L., San Diego, CA, UNITED STATES
Ahlem, Clarence N., San Diego, CA, UNITED STATES
Auci, Dominick L., San Diego, CA, UNITED STATES
Dowding, Charles, San Diego, CA, UNITED STATES
Frincke, James M., San Diego, CA, UNITED STATES
Li, Mei, San Diego, CA, UNITED STATES
Page, Theodore M., Carlsbad, CA, UNITED STATES
Stickney, Dwight R., Granite Bay, CA, UNITED STATES
Trauger, Richard J., Leucadia, CA, UNITED STATES
White, Steven K., San Diego, CA, UNITED STATES
PI US 2004138187 A1 20040715
AI US 2003-651515 A1 20030828 (10)
PRAI US 2002-407146P 20020828 (60)
US 2002-408332P 20020904 (60)
US 2003-479257P 20030617 (60)
DT Utility
FS APPLICATION
LREP HOLLIS-EDEN PHARMACEUTICALS, INC., 4435 EASTGATE MALL, SUITE 400, SAN
DIEGO, CA, 92121
CLMN Number of Claims: 37
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 16128
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 4 OF 5 USPATFULL on STN
AB The invention relates to the use of compounds to treat a number of
conditions, such as thrombocytopenia, neutropenia or the delayed effects
of radiation therapy. Compounds that can be used in the invention
include methyl-2,3,4-trihydroxy-1-O-(7,17-dioxoandrost-5-ene-3 β -yl)-
 β -D-glucopyranosiduronate, 16 α ,3 α -dihydroxy-5 α -
androstan-17-one or 3,7,16,17-tetrahydroxyandrost-5-ene,
3,7,16,17-tetrahydroxyandrost-4-ene,3,7,16,17-tetrahydroxyandrost-1-ene
or 3,7,16,17-tetrahydroxyandrostane that can be used in the treatment
method.
AN 2003:120747 USPATFULL
TI Blood cell deficiency treatment method
IN Ahlem, Clarence N., San Diego, CA, UNITED STATES
Reading, Christopher, San Diego, CA, UNITED STATES
Frincke, James, San Diego, CA, UNITED STATES
Stickney, Dwight, Granite Bay, CA, UNITED STATES
Lardy, Henry A., Madison, WI, UNITED STATES
Marwah, Padma, Middleton, WI, UNITED STATES
Marwah, Ashok, Middleton, WI, UNITED STATES
Prendergast, Patrick T., Straffan, IRELAND
PI US 2003083231 A1 20030501
AI US 2002-87929 A1 20020301 (10)
RLI Continuation-in-part of Ser. No. US 2000-675470, filed on 28 Sep 2000,
PENDING Continuation-in-part of Ser. No. US 2001-820483, filed on 29 Mar
2001, PENDING Continuation-in-part of Ser. No. US 2000-535675, filed on
23 Mar 2000, PENDING Continuation-in-part of Ser. No. US 1999-449004,
filed on 24 Nov 1999, ABANDONED Continuation-in-part of Ser. No. US
1999-449184, filed on 24 Nov 1999, ABANDONED Continuation-in-part of
Ser. No. US 1999-449042, filed on 24 Nov 1999, ABANDONED

Continuation-in-part of Ser. No. US 1999-461026, filed on 15 Dec 1999,
ABANDONED Continuation-in-part of Ser. No. US 2000-586673, filed on 1
Jun 2000, ABANDONED Continuation-in-part of Ser. No. US 2000-586672,
filed on 1 Jun 2000, ABANDONED Continuation-in-part of Ser. No. US
1999-414905, filed on 8 Oct 1999, ABANDONED

PRAI US 1999-161453P 19991025 (60)
US 2001-272624P 20010301 (60)
US 2001-323016P 20010911 (60)
US 2001-340045P 20011130 (60)
US 2001-328738P 20011011 (60)
US 2001-338015P 20011108 (60)
US 2001-343523P 20011220 (60)
US 1999-126056P 19991019 (60)
US 1999-124087P 19990311 (60)
US 1998-109923P 19981124 (60)
US 1998-109924P 19981124 (60)
US 1998-110127P 19981127 (60)
US 1998-112206P 19981215 (60)
US 1999-145823P 19990727 (60)
US 1999-137745P 19990603 (60)
US 1999-140028P 19990616 (60)

DT Utility

FS APPLICATION

LREP HOLLIS-EDEN PHARMACEUTICALS, INC., 4435 EASTGATE MALL, SUITE 400, SAN
DIEGO, CA, 92121

CLMN Number of Claims: 45

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 19428

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 5 USPATFULL on STN

AB The invention relates generally to compositions of and methods for
obtaining ubiquitous, nuclear receptor (UR) polypeptides. The invention
also relates to polynucleotides encoding UR polypeptides, recombinant
host cells and vectors containing UR-encoding polynucleotide sequences,
and recombinant UR polypeptides. By way of example, the invention
discloses the cloning and functional expression of at least two
different UR polypeptides. The invention also includes methods for using
the isolated, recombinant receptor polypeptides in assays designed to
select substances which interact with UR polypeptides for use in
diagnostic, drug design and therapeutic applications.

AN 97:51869 USPATFULL

TI Isolated nucleic acid encoding a ubiquitous nuclear receptor

IN Liao, Shutsung, Chicago, IL, United States

Song, Ching, Durham, NC, United States

PA Arch Development Corporation, Chicago, IL, United States (U.S.
corporation)

PI US 5639616 19970617

AI US 1994-342411 19941118 (8)

RLI Continuation-in-part of Ser. No. US 1993-152003, filed on 10 Nov 1993,
now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Walsh, Stephen G.; Assistant Examiner: Ulm, John D.

LREP Arnold White & Durkee

CLMN Number of Claims: 17

ECL Exemplary Claim: 1

DRWN 21 Drawing Figure(s); 18 Drawing Page(s)

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LN.CNT 4472

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> index bioscience

FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

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SESSION

FULL ESTIMATED COST

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22.73

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS,
BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB,
CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 13:33:39 ON 08 NOV 2004

75 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> Bcl-2 and NMR and apoptosis

1 FILE ADISINSIGHT

2 FILE AGRICOLA

1 FILE BIOENG

22 FILE BIOSIS

0* FILE BIOTECHABS

13 FILES SEARCHED...

2 FILE BIOTECHDS

8 FILE BIOTECHNO

10 FILE CANCERLIT

29 FILE CAPLUS

1 FILE CEABA-VTB

1 FILE CIN

3 FILE DDFU

3 FILE DISSABS

5 FILE DRUGU

21 FILE EMBASE

33 FILES SEARCHED...

15 FILE ESBIODASE

3 FILE FEDRIP

1 FILE FSTA

6 FILE IFIPAT

4 FILE JICST-EPLUS

6 FILE LIFESCI

25 FILE MEDLINE

3 FILE NTIS

7 FILE PASCAL

55 FILES SEARCHED...

1 FILE PROMT

44 FILE SCISEARCH

8 FILE TOXCENTER

466 FILE USPATFULL

44 FILE USPAT2

2 FILE WPIDS

73 FILES SEARCHED...

2 FILE WPINDEX

30 FILES HAVE ONE OR MORE ANSWERS, 75 FILES SEARCHED IN STNINDEX

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L6 QUE BCL-2 AND NMR AND APOPTOSIS

=>

=>

=>

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=> d rank

F1	466	USPATFULL
F2	44	SCISEARCH
F3	44	USPAT2
F4	29	CAPLUS
F5	25	MEDLINE
F6	22	BIOSIS
F7	21	EMBASE
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F9	10	CANCERLIT
F10	8	BIOTECHNO
F11	8	TOXCENTER
F12	7	PASCAL
F13	6	IFIPAT
F14	6	LIFESCI
F15	5	DRUGU
F16	4	JICST-EPLUS
F17	3	DDFU
F18	3	DISSABS
F19	3	FEDRIP
F20	3	NTIS
F21	2	AGRICOLA
F22	2	BIOTECHDS
F23	2	WPIDS
F24	2	WPINDEX
F25	1	ADISINSIGHT
F26	1	BIOENG
F27	1	CEABA-VTB
F28	1	CIN
F29	1	FSTA
F30	1	PROMT

=> file biosis medline caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

10.83

33.56

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FILE 'CAPLUS' ENTERED AT 13:45:05 ON 08 NOV 2004

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=> Bcl-2 and NMR and apoptosis

L7 76 BCL-2 AND NMR AND APOPTOSIS

=> dup remove

ENTER L# LIST OR (END):17

PROCESSING COMPLETED FOR L7

L8 43 DUP REMOVE L7 (33 DUPLICATES REMOVED)

=> d ti 1-23

L8 ANSWER 1 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

TI Conversion of apoptotic proteins

L8 ANSWER 2 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

TI Methods of identifying agents that alter association of Bit1 and AES, alter Bcl-2 transcription, and/or modulate cell death, and therapeutic uses

L8 ANSWER 3 OF 43 MEDLINE on STN

TI Conformation of membrane-associated proapoptotic tBid.

L8 ANSWER 4 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

TI Changes in phosphate metabolism in thymoma cells suggest mechanisms for resistance to dexamethasone-induced apoptosis. A 31P NMR spectroscopic study of cell extracts. [Erratum to document cited in CA138:036909]

L8 ANSWER 5 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

TI Solution Conformations of Wild-Type and Mutated Bak BH3 Peptides via Dynamical Conformational Sampling and Implication to Their Binding to Antiapoptotic Bcl-2 Proteins

L8 ANSWER 6 OF 43 MEDLINE on STN

DUPLICATE 1

TI Targeting apoptosis via chemical design: inhibition of bid-induced cell death by small organic molecules.

L8 ANSWER 7 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

DUPLICATE 2

TI Divergence of Genbank and human tumor Bcl-2 sequences and implications for binding affinity to key apoptotic proteins.

L8 ANSWER 8 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

DUPLICATE 3

TI Localization of dynein light chains 1 and 2 and their pro-apoptotic ligands.

L8 ANSWER 9 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

DUPLICATE 4

TI Rational design and real time, in-cell detection of the proapoptotic activity of a novel compound targeting Bcl-XL.

L8 ANSWER 10 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

DUPLICATE 5

TI Small-molecule inhibitors of Bcl-2 protein.

L8 ANSWER 11 OF 43 MEDLINE on STN

DUPLICATE 6

TI Structural studies of apoptosis and ion transport regulatory proteins in membranes.

- L8 ANSWER 12 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 7
TI Defining the p53 DNA-binding domain/Bcl-xL-binding interface using
NMR.
- L8 ANSWER 13 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 8
TI Overexpression of catalase or Bcl-2 alters glucose and
energy metabolism concomitant with dexamethasone resistance.
- L8 ANSWER 14 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Humanin protein interactions with Bax and Bid and their use for
identifying modulators of **apoptosis**
- L8 ANSWER 15 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Solution Structure of Human BCL-w: Modulation of Ligand Binding by the
C-Terminal Helix
- L8 ANSWER 16 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Discovery, Characterization, and Structure-Activity Relationships Studies
of Proapoptotic Polyphenols Targeting B-Cell Lymphocyte/Leukemia-2
Proteins
- L8 ANSWER 17 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Cyclic AMP reverses radiocontrast media-induced **apoptosis** in
LLC-PK1 cells by activating A kinase/PI3 kinase
- L8 ANSWER 18 OF 43 MEDLINE on STN
TI Unique structural features of a BCL-2 family protein
CED-9 and biophysical characterization of CED-9/EGL-1 interactions.
- L8 ANSWER 19 OF 43 MEDLINE on STN
TI Solution structure of the BHRF1 protein from Epstein-Barr virus, a homolog
of human Bcl-2.
- L8 ANSWER 20 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN
TI Interaction of BID, a pro-apoptotic BCL-2 family
member, with lipid membranes: A site-directed spin labeling Study.
- L8 ANSWER 21 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 9
TI Overexpression of catalase or Bcl-2 delays or prevents
alterations in phospholipid metabolism during glucocorticoid-induced
apoptosis in WEHI7.2 cells.
- L8 ANSWER 22 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 10
TI Structure determination, **apoptosis** induction, and telomerase
inhibition of CFP-2, a novel lichenin from Cladonia furcata.
- L8 ANSWER 23 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN
TI Novel chemically-stabilized helices of the BCL-2
family induce **apoptosis** of leukemia cells.

=> d ab bib 23

- L8 ANSWER 23 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
- AB Faulty regulation of apoptotic pathways is a seminal event in the pathogenesis of a wide variety of hematologic, oncologic, and other diseases. **Apoptosis** is governed by the **BCL-2** family of pro- and anti-apoptotic proteins, which form a complex network of checks and balances that dictate cell fate. **BCL-2**, for example, is a survival protein whose overproduction can facilitate pathologic cell survival. Anti-apoptotic proteins, such as **BCL-2** and **BCL-XL**, and pro-apoptotic proteins, such as **BAK** and **BAX**, share sequence conservation in multiple "**BCL-2** homology" (BH) domains. These "multidomain" apoptotics exert their roles as guardian or executioner at mitochondrial and endoplasmic reticulum membranes, receiving regulatory signals from another class of pro-apoptotic proteins, characterized by homology in the BH3-domain only. Deletion and mutagenesis studies determined that the amphipathic alpha-helical BH3 segment of pro-apoptotic family members functions as a critical death domain. Whereas peptides modeled after BH3 domains retain select in vitro biochemical activities, their in vivo utility is compromised by loss of helical secondary structure, susceptibility to proteolytic degradation, and inability to penetrate intact cells. We developed and applied a chemical strategy for generating highly specific and stable peptidic compounds that preserve both the primary and secondary structure of biologically active apoptotic peptides, in order to maximize their potential as therapeutic reagents and as in vivo biological tools to elucidate apoptotic pathways. We employed a synthetic crosslinking strategy to generate a panel of "Stabilized Alpha-Helices of BH3-domains" or SAHBs modeled after the BH3 domain of BID, a pro-apoptotic family member capable of activating mitochondrial cell death through interactions with both pro- and anti-apoptotic multidomain proteins. Circular dichroism studies revealed dramatic enhancement of SAHB secondary structure in solution, with several compounds displaying a more than 5-fold increase in percent helicity compared to the unmodified BID BH3 peptide. SAHBs are likewise more resistant to proteolytic degradation as determined by trypsin digestion kinetic analyses. In in vitro binding assays, SAHBs display increased **BCL-2** binding affinity. Two-dimensional 1H-15N Heteronuclear Single Quantum Correlation Nuclear Magnetic Resonance (HSQC NMR) spectra confirmed that SAHBs specifically engage the physiologic BH3-binding site of multidomain anti-apoptotic proteins. SAHBs induce rapid release of cytochrome c from purified mouse liver mitochondria, but have no effect on mitochondria lacking BAK/BAX, confirming the specificity of SAHB activity in triggering mitochondrial **apoptosis**. The cell permeability of SAHBs was demonstrated by tracking fluorescein-labeled SAHBs in cultured cells by FACS analysis and confocal microscopy. Furthermore, SAHBs activate **apoptosis** in cultured B-, T-, and mixed-lineage leukemia cells. The specificity of SAHB activity in inducing leukemia cell **apoptosis** was confirmed by the inability of mutant SAHBs, incorporating a single point mutation known to abolish BH3-domain activity, to have any effect on the cultured cells. These data indicate that SAHBs have the potential to serve as biological tools to dissect and manipulate apoptotic pathways in vivo in normal and malignant cells.
- AN 2004:180831 BIOSIS
- DN PREV200400180880
- TI Novel chemically-stabilized helices of the **BCL-2** family induce **apoptosis** of leukemia cells.
- AU Walensky, Loren D. [Reprint Author]; Escher, Iris; Malia, Thomas J.; Wagner, Gerhard; Verdine, Gregory L.; Korsmeyer, Stanley J.

CS Department of Pediatric Hematology/Oncology, Dana Farber Cancer
Institute/Children's Hospital Boston, Harvard Medical School, Boston, MA,
USA
SO Blood, (November 16 2003) Vol. 102, No. 11, pp. 5a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology.
San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004

=> d ti 43-23

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=> d ti 23-43

L8 ANSWER 23 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN

TI Novel chemically-stabilized helices of the BCL-2
family induce **apoptosis** of leukemia cells.

L8 ANSWER 24 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

TI Phospholipid scramblase transport system-based method for targeting
chemical compounds to cells, pharmaceutical compositions, and therapeutic
and diagnostic use

L8 ANSWER 25 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of amino acid derivatives used as perturbed membrane-binding
compounds for diagnostic and therapeutic applications

L8 ANSWER 26 OF 43 MEDLINE on STN

TI The apoptotic protein tBid promotes leakage by altering membrane
curvature.

L8 ANSWER 27 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 11

TI Novel polyphenol molecule isolated from licorice root (Glycyrrhiza glabra)
induces **apoptosis**, G2/M cell cycle arrest, and Bcl-

2 phosphorylation in tumor cell lines.

- L8 ANSWER 28 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN
TI A view to a kill: Ligands for **Bcl-2** family proteins.
- L8 ANSWER 29 OF 43 MEDLINE on STN DUPLICATE 12
TI Changes in phosphate metabolism in thymoma cells suggest mechanisms for
resistance to dexamethasone-induced **apoptosis**. A ³¹P NMR
spectroscopic study of cell extracts.
- L8 ANSWER 30 OF 43 MEDLINE on STN
TI Backbone dynamics of the 8 kDa dynein light chain dimer reveals molecular
basis of the protein's functional diversity.
- L8 ANSWER 31 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 13
TI Novel substituted methylenedioxy lignan suppresses proliferation of cancer
cells by inhibiting telomerase and activation of c-myc and caspases
leading to **apoptosis**.
- L8 ANSWER 32 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 14
TI What's in the 'BAG'? A functional domain analysis of the BAG-family
proteins.
- L8 ANSWER 33 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 15
TI Discovery of small-molecule inhibitors of **Bcl-2**
through structure-based computer screening.
- L8 ANSWER 34 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN
TI Bax and other pro-apoptotic **Bcl-2** family
"killer-proteins" and their victim, the mitochondrion.
- L8 ANSWER 35 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 16
TI Identification of small-molecule inhibitors of interaction between the BH3
domain and Bcl-xL.
- L8 ANSWER 36 OF 43 MEDLINE on STN
TI NMR studies of the anti-apoptotic protein Bcl-xL in micelles.
- L8 ANSWER 37 OF 43 MEDLINE on STN
TI Rationale for Bcl-xL/Bad peptide complex formation from structure,
mutagenesis, and biophysical studies.
- L8 ANSWER 38 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN
TI Targeting the mitochondrial redox state of leukemia and lymphoma cells
with PK11195 for effective therapy.
- L8 ANSWER 39 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN
TI Assessing pore formation by **BCL-2** during
apoptosis in cell lines and human leukemic cells: Cysteine 158 in
the alpha 5 helical loop is in an aqueous environment.

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- L8 ANSWER 40 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 17
- TI Refolding, purification, and characterization of a loop deletion mutant of
human Bcl-2 from bacterial inclusion bodies.
- L8 ANSWER 41 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 18
- TI Recombinant mouse Bcl-2-(1-203): Two domains connected
by a long protease-sensitive linker.
- L8 ANSWER 42 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 19
- TI Detection of apoptotic cell death by proton nuclear magnetic resonance
spectroscopy.
- L8 ANSWER 43 OF 43 MEDLINE on STN
- TI X-ray and NMR structure of human Bcl-xL, an inhibitor of
programmed cell death.

=> d ti 29, 34, 37, 42, 43

- L8 ANSWER 29 OF 43 MEDLINE on STN DUPLICATE 12
- TI Changes in phosphate metabolism in thymoma cells suggest mechanisms for
resistance to dexamethasone-induced apoptosis. A 31P NMR
spectroscopic study of cell extracts.
- L8 ANSWER 34 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN
- TI Bax and other pro-apoptotic Bcl-2 family
"killer-proteins" and their victim, the mitochondrion.
- L8 ANSWER 37 OF 43 MEDLINE on STN
- TI Rationale for Bcl-xL/Bad peptide complex formation from structure,
mutagenesis, and biophysical studies.
- L8 ANSWER 42 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 19
- TI Detection of apoptotic cell death by proton nuclear magnetic resonance
spectroscopy.
- L8 ANSWER 43 OF 43 MEDLINE on STN
- TI X-ray and NMR structure of human Bcl-xL, an inhibitor of
programmed cell death.

=> d ab bib 29, 34, 37, 42, 43

- L8 ANSWER 29 OF 43 MEDLINE on STN DUPLICATE 12
- AB Treatment of the mouse thymoma-derived WEHI7.2 cell line with
dexamethasone, a synthetic glucocorticoid, causes the cells to undergo
apoptosis. Previous studies have shown that WEHI7.2 cell variants
with an increased antioxidant defense exhibit increased resistance to
dexamethasone-induced apoptosis, suggesting that oxidative
stress may play a role in glucocorticoid-induced apoptosis. In
this work we compared metabolic profiles of WEHI7.2 parental cells with
those of WEHI7.2 variants with an increased antioxidant defense or
overexpressing bcl-2, to determine whether bolstering
the antioxidant defense results in altered metabolic parameters that could

translate into increased resistance to dexamethasone-induced **apoptosis**. WEHI7.2 parental cells and cells overexpressing catalase, thioredoxin or **bcl-2**, or selected for resistance to 200 micro M H₂O₂ were cultured in low-glucose DMEM medium supplemented with 10% calf serum, and extracted using chloroform-methanol-water (1:1:1). Metabolites contained in the aqueous and organic phases of the extracts were processed separately and subjected to high-resolution (31)P NMR spectroscopy. In most of the steroid-resistant variants, ATP levels and energetic status were decreased compared with the steroid-sensitive parental cell line, while the concentrations of hexose and triose phosphates were increased. Furthermore, the ratio of choline-containing phospholipids to ethanolamine-containing phospholipids was generally reduced in steroid-resistant cells. Phosphatidylethanolamine and its derivatives contain a higher amount of polyunsaturated fatty acids (PUFA) than the choline-containing analogs, and PUFA are readily oxidized by reactive oxygen species. Therefore, an increased initial amount of phosphatidylethanolamine may increase the 'buffering capacity' of this antioxidant and may thus contribute to the steroid resistance of WEHI7.2 variants.

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AN 2002444772 MEDLINE

DN PubMed ID: 12203227

TI Changes in phosphate metabolism in thymoma cells suggest mechanisms for resistance to dexamethasone-induced **apoptosis**. A 31P NMR spectroscopic study of cell extracts.

AU Lutz N W; Tome M E; Aiken N R; Briehl M M

CS Arizona Cancer Center, PO Box 245024, University of Arizona, Tucson, AZ 85724, USA.

NC CA 09213 (NCI)

CA 71768 (NCI)

CA 80130 (NCI)

SO NMR in biomedicine, (2002 Aug) 15 (5) 356-66.

Journal code: 8915233. ISSN: 0952-3480.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200303

ED Entered STN: 20020831

Last Updated on STN: 20030321

Entered Medline: 20030320

L8 ANSWER 34 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

AB Two major intracellular **apoptosis** signaling cascades have been characterized, the mitochondrial pathway and the death receptor pathway. The mitochondrial pathway is regulated by members of the Bcl-2 protein family. The members of this family can be subdivided into anti- and pro-apoptotic proteins. The pro-apoptotic members are further divided into two groups, the multidomain and the 'BH3 domain only' proteins. When cells are exposed to apoptotic stimulation, pro-apoptotic proteins are activated through post-translational modifications or changes in their conformation. The main site of action of the multidomain proteins are the mitochondria, where these proteins induce permeabilization of the outer membrane resulting in the release of proteins, including cytochrome c, from the intermembrane space. In the cytosol cytochrome c activates caspase cascades ultimately leading to cell death. Mounting evidence indicates that **apoptosis** is involved

in a wide range of pathological conditions. Recent studies suggest that the mitochondrial signaling pathway is involved in several diseases. Although, so far, with the exception of *C. elegans*, most studies on **apoptosis** have been performed in mammalian systems, recently homologues to the **Bcl-2** family members, including pro-apoptotic members, have been identified in *Drosophila* and zebrafish. Here the structure and function of the various pro-apoptotic **Bcl-2** family members, their effects on mitochondria, and their involvement in diseases are discussed.

AN 2002:270954 BIOSIS
 DN PREV200200270954
 TI Bax and other pro-apoptotic **Bcl-2** family
 "killer-proteins" and their victim, the mitochondrion.
 AU Antonsson, Bruno [Reprint author]
 CS Serono Pharmaceutical Research Institute, 14, chemin des Aulx, 1228
 Plan-les-Ouates, Geneva, Switzerland
 bruno.antonsson@serono.com
 SO Cell and Tissue Research, (December, 2001) Vol. 306, No. 3, pp. 347-361.
 print.
 CODEN: CTSRCS. ISSN: 0302-766X.
 DT Article
 General Review; (Literature Review)
 LA English
 ED Entered STN: 1 May 2002
 Last Updated on STN: 1 May 2002

L8 ANSWER 37 OF 43 MEDLINE on STN
 AB The three-dimensional structure of the anti-apoptotic protein Bcl-xL complexed to a 25-residue peptide from the death promoting region of Bad was determined using **NMR** spectroscopy. Although the overall structure is similar to Bcl-xL bound to a 16-residue peptide from the Bak protein (Sattler et al., 1997), the Bad peptide forms additional interactions with Bcl-xL. However, based upon site-directed mutagenesis experiments, these additional contacts do not account for the increased affinity of the Bad 25-mer for Bcl-xL compared to the Bad 16-mer. Rather, the increased helix propensity of the Bad 25-mer is primarily responsible for its greater affinity for Bcl-xL. Based on this observation, a pair of 16-residue peptides were designed and synthesized that were predicted to have a high helix propensity while maintaining the interactions important for complexation with Bcl-xL. Both peptides showed an increase in helix propensity compared to the wild-type and exhibited an enhanced affinity for Bcl-xL.

AN 2001300585 MEDLINE
 DN PubMed ID: 11206074 ✓
 TI Rationale for Bcl-xL/Bad peptide complex formation from structure, mutagenesis, and biophysical studies.
 AU Petros A M; Nettesheim D G; Wang Y; Olejniczak E T; Meadows R P; Mack J; Swift K; Matayoshi E D; Zhang H; Thompson C B; Fesik S W
 CS Pharmaceutical Discovery Division, Abbott Laboratories, Abbott Park, Illinois 60064-6098, USA.
 SO Protein science : a publication of the Protein Society, (2000 Dec) 9 (12) 2528-34.
 Journal code: 9211750. ISSN: 0961-8368.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200105
 ED Entered STN: 20010604

Last Updated on STN: 20010604
Entered Medline: 20010531

- L8 ANSWER 42 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 19
- AB Cells undergoing **apoptosis** (programmed cell death) display
profound morphologic and biochemical changes in the nucleus, cytoplasm,
and plasma membrane. We have shown a direct temporal relationship between
the onset of **apoptosis** in Jurkat T-cell lymphoblast cultures and
a greater than twofold increase in the signal intensity of the methylene
resonance (at 1.3 ppm) as observed by proton nuclear magnetic resonance
spectroscopy (1H NMR). The increase in the methylene resonance
intensity was seen when **apoptosis** was induced by serum
deprivation, glucocorticoid, and doxorubicin treatment but not in necrotic
(nonapoptotic) cell death. We have found similar changes in a variety of
other cell lines undergoing **apoptosis** including the Hut 78
T-cell leukemia, JY natural killer T-cell leukemia, Daudi B-cell lymphoma,
HeLa, and 3T3 fibroblast cell lines. Furthermore, this spectral change
was diminished in Bcl-2 overexpressing HL-60 cell
cultures treated with doxorubicin, which were relatively resistant to
apoptosis, as compared to apoptotic HL-60 cultures. 1H NMR
spectroscopy therefore may be useful in detecting apoptotic cell death in
vivo.
- AN 1996:125822 BIOSIS
DN PREV199698697957
TI Detection of apoptotic cell death by proton nuclear magnetic resonance
spectroscopy.
AU Blankenberg, Francis G. [Reprint author]; Storrs, Richard W.; Naumovski,
Louie; Goralski, Thomas; Spielman, Daniel
CS Lucile Salter Packard Child. Hosp., Dep. Radiol., 725 Welch Rd., Palo
Alto, CA 94304, USA
SO Blood, (1996) Vol. 87, No. 5, pp. 1951-1956.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Article
LA English
ED Entered STN: 27 Mar 1996
Last Updated on STN: 27 Mar 1996
- L8 ANSWER 43 OF 43 MEDLINE on STN
- AB THE Bcl-2 family of proteins regulate programmed cell
death by an unknown mechanism. Here we describe the crystal and solution
structures of a Bcl-2 family member, Bcl-xL (reference 2).
The structures consist of two central, primarily hydrophobic
alpha-helices, which are surrounded by amphipathic helices. A 60-residue
loop connecting helices alpha1 and alpha2 was found to be flexible and
non-essential for anti-apoptotic activity. The three functionally
important Bcl-2 homology regions (BH1, BH2 and BH3)
are in close spatial proximity and form an elongated hydrophobic cleft
that may represent the binding site for other Bcl-2
family members. The arrangement of the alpha-helices in Bcl-xL is
reminiscent of the membrane translocation domain of bacterial toxins, in
particular diphtheria toxin and the colicins. The structural similarity
may provide a clue to the mechanism of action of the Bcl-
2 family of proteins.
- AN 96256675 MEDLINE
DN PubMed ID: 8692274
TI X-ray and NMR structure of human Bcl-xL, an inhibitor of
programmed cell death.
AU Muchmore S W; Sattler M; Liang H; Meadows R P; Harlan J E; Yoon H S;

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Nettesheim D; Chang B S; Thompson C B; Wong S L; Ng S L; Fesik S W
CS Protein Crystallography, Pharmaceutical Discovery Division, Abbott
Laboratories, Abbott Park, Illinois 60064, USA.
SO Nature, (1996 May 23) ~~381 (6580) 335-41.~~
Journal code: 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS PDB-1LXL; PDB-1MAZ
EM 199608
ED Entered STN: 19960911
Last Updated on STN: 19960911
Entered Medline: 19960823